

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

PAR PHARMACEUTICAL, INC., and ENDO)
PAR INNOVATION COMPANY, LLC,)

Plaintiffs,)

v.)

ZYDUS PHARMACEUTICALS (USA) INC.)
and ZYDUS LIFESCIENCES LTD.,)

Defendant.)

C.A. No. 23-cv-866-RGA-LDH

**PLAINTIFFS' BRIEF IN SUPPORT OF MOTION FOR
TEMPORARY RESTRAINING ORDER, PRELIMINARY
INJUNCTION AND EXPEDITED DISCOVERY**

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INTRODUCTION

Plaintiffs Par Pharmaceutical, Inc. and Endo Par Innovation Company, LLC (collectively “Par”) move this Court, with notice to Zydus' counsel, for a temporary restraining order and preliminary injunction barring defendants Zydus Pharmaceuticals (USA) Inc. (“Zydus USA”) and Zydus Lifesciences Ltd. (“Zydus Lifesciences”) (collectively “Zydus”) from continuing to import and sell generic varenicline tartrate tablets due to their infringement of U.S. Patent No. 11,717,524 (the “’524 Patent”), which issued today.

Varenicline is used as a smoking cessation treatment to reduce the craving for nicotine. The original branded product, CHANTIX®, was marketed by Pfizer, but was withdrawn from the market in July 2021, following the discovery that it contained high levels of nitrosamines, a potentially carcinogenic impurity. Par undertook extensive research to detect, identify, quantify, and control the varenicline-related nitrosamine impurities that were present in its varenicline tablets, which were still under development at that time. Par developed a process for producing the first low nitrosamine varenicline tablets, obtained FDA approval, and brought its low nitrosamine varenicline tablets to the market.

Par filed a patent application on its process, and the United States Patent and Trademark Office (“PTO”) just granted the ’524 patent to Par. The ’524 patent claims a novel, elegant, and commercially practicable method for reducing nitrosamines to levels well below the FDA’s acceptable intake limits.

At about the same time Par heard from the PTO that the application leading to the ’524 patent would be granted, Par learned that Zydus was planning to launch a competing product. Par sent multiple letters notifying Zydus of its patent rights, pointed Zydus to the application at the PTO, advised Zydus that Par had paid the applicable issue fee and that the PTO would be issuing the forthcoming ’524 patent within two months. Par believes it is likely that Zydus is

using the patented manufacturing methods to make the Zydus tablets and therefore asked multiple times for Zydus to state whether it disagreed, and if so, to provide supporting documentation. Zydus ignored Par's requests and instead launched its generic varenicline tablets with full knowledge of Par's expected patent rights. Par's hands have been tied until today when the '524 patent issued.

Zydus's launch is inflicting severe and irreparable harm on Par at a particularly critical and tenuous time in the life of the company. Par, along with its parent company (Endo International plc ("Endo")) and corporate affiliates, filed voluntary petitions for relief under the Bankruptcy Code and are seeking to emerge from bankruptcy via a sale of the company to senior debtholders. Varenicline is a major product for Par, and the revenues from the product are crucial to its future business goals and reorganization plans.

Under these circumstances, each of the well-established four-factor balancing standards for the issuance of preliminary injunctive relief favor Par:

First, to satisfy the likelihood of success factor, Par need only demonstrate "a reasonable chance, or probability, of winning" regarding liability for patent infringement. *Singer Mgmt. Consultants, Inc. v. Milgram*, 650 F.3d 223, 229 (3d Cir. 2011) (en banc). Par brings this case under 35 U.S.C. §§ 271(g) and 295, which govern patent claims relating to the use of a manufacturing process outside the U.S. In enacting § 295, Congress anticipated the infringement issue in this case by flipping the burden of proof to the defendant when an alleged infringer manufactures outside the United States, brings the product into the country, and then refuses to provide information on the foreign manufacturing process. Here, Zydus has refused to grant Par access to its ANDA in an attempt to use the delay inherent in the litigation process to steal

market share. Par has been unable, after a reasonable effort, to obtain the details of the Zydus process, and accordingly, a presumption arises that Zydus' product infringes the '524 patent.

Second, Zydus's sales of the accused tablets, if unchecked, will inflict severe and irreparable harm on Par and Endo, including significant and unrecoverable price erosion and lost market share, as well as potential impairment of their ability to fund ongoing research and development (R&D), to support planned new product launches, to fund employee salaries and other overhead expenses at current levels, and to pay debt obligations and obtain additional capital as needed for ongoing business operations.

Third, these substantial and irreparable harms to Par would vastly exceed the consequences to Zydus of a temporary pause in the sales of the accused tablets, giving Par and the Court a proper opportunity to evaluate Zydus's suspected infringement and ensure that Zydus is not treading upon Par's patent rights. At most, Zydus will temporarily forego some profit, which can be addressed with the provision of adequate security in accordance with Rule 65.

Finally, the public interest also favors entry of the requested relief and restoration of the status quo that existed at the time Par notified Zydus of its patent rights. There is a significant public interest in protecting Par's intellectual property rights and investment in R&D—and this interest outweighs any benefit Zydus may attribute to its generic product.

FACTUAL AND PROCEDURAL BACKGROUND

A. FDA Guidances Concerning Nitrosamine Impurities

In recent years, the Food and Drug Administration ("FDA") has become increasingly concerned about high levels of nitrosamine impurities that it began seeing in pharmaceutical drug products. "Nitrosamines" are a class of potentially carcinogenic impurities that can arise during the manufacture of drug products. *See, e.g.*, Declaration of Dr. David Dodds ("Dodds

Decl.”), ¶ 11.; Ex. 2¹ at 3-5. The discovery of unacceptably high levels of nitrosamines in multiple drug products led the FDA to release guidances, beginning in 2020, concerning the control of nitrosamine impurities which “recommend[] steps manufacturers of APIs [active pharmaceutical ingredients] and drug products should take to detect and prevent unacceptable levels of nitrosamine impurities in pharmaceutical products.” Dodds Decl., ¶ 12.; Ex. 2 at 3-5.

Varenicline tartrate is a synthetic drug substance used in the treatment of nicotine dependency, addiction, and withdrawal. Dodds Decl., ¶ 10. It has been sold in the United States since 2006, when Pfizer launched its varenicline tartrate tablets under the tradename CHANTIX®. *Id.* In September 2020, as part of the ongoing investigation and guidances regarding nitrosamine impurities noted above, the FDA established an acceptable daily intake limit for varenicline-related nitrosamine impurities of 37 nanograms, which equates to 18.5 parts per million (“ppm”) of those impurities. *See id.*, ¶ 13; Ex. 3.

Not long thereafter, Pfizer discovered the presence of nitrosamine impurities in its CHANTIX® tablets at levels above FDA’s acceptable intake limit, ultimately causing Pfizer to discontinue all sales of CHANTIX®. *See, e.g.*, Ex. 10; 88 Fed. Reg. 12384 (Feb. 27, 2023). Notwithstanding the fact that CHANTIX® was a blockbuster drug with more than \$1 billion in annual sales at its peak (Declaration of Mark Bradley (“Bradley Decl.”), ¶ 7), to date, Pfizer has not been able to come to market with reformulated CHANTIX® tablets that comply with the FDA-mandated acceptable daily nitrosamine intake limits.

B. Par Scientists Develop Varenicline Tartrate Products With Nitrosamine Levels Well Below the FDA’s Daily Intake Limit

When Par began development work on its varenicline tartrate tablets, there was no

¹ All exhibit references refer to exhibits to the declaration of Robert D. Rhoad, filed herewith.

published literature about the presence of nitrosamine impurities in varenicline products, the specific chemical structure of any such impurities, or how to detect them. Accordingly, Par had to develop its own methods to identify, quantify, and control any nitrosamines present in its tablets. Par's scientists worked hard to develop analytical methods to identify, detect, and quantify the nitrosamine impurities in its varenicline API, as well as a commercially practicable method to reduce those impurities to acceptable levels.

Par succeeded: it developed a varenicline tablet that has remarkably low levels of nitrosamine impurities. *See, e.g.,* Dodds Decl., ¶¶ 15-17; '524 patent (Ex. 1) at Table 23. As shown by the FDA's own testing, Par's tablets have a tiny fraction of the nitrosamines found in CHANTIX® (3 ppm vs. 155-474 ppm) and fall well below the FDA's intake limit. *See* Ex. 3. Accordingly, on August 11, 2021, the FDA approved Par's application to sell generic varenicline tartrate tablets. Because the nitrosamine levels in others' varenicline tartrate tablet products exceeded the FDA's acceptable daily intake limit, each of those products was withdrawn from the market, leaving Par for a period as the only manufacturer approved to sell varenicline tartrate products in the United States. *See, e.g.,* Ex. 10; Bradley Decl., ¶ 13.

As the first manufacturer able to overcome the difficulties associated with developing varenicline tablets with nitrosamine impurities below the FDA's acceptable daily intake level, which other manufacturers like Pfizer have been unable to do, Par sought patents on the novel manufacturing methods it developed. Earlier today, the PTO issued the '524 Patent, titled "Varenicline Compound and Process of Manufacture Thereof." Ex. 1. Representative claim 1 recites the following:

1. A method of making a varenicline tartrate tablet comprising less than 50 ppm of nitrosamine impurities, the method comprising:
 - (a) mixing varenicline free base with tartaric acid to form varenicline tartrate
 - (b) means for reducing the nitrosamine impurities to less than 50 ppm per

tablet as measured by LC-ESI-HRMS Method;
wherein the means comprises an acid-base treatment.

C. Zydus's Suspected Infringement of the '524 Patent

Par became aware that Zydus had submitted an ANDA seeking approval to sell generic varenicline tartrate tablets ("Zydus's Tablets") and wrote Zydus multiple times to advise Zydus of its issued patents and pending patent application. After Zydus ignored Par's first notice letter, dated May 17, 2023 (Ex. 4), Par sent a second letter on June 9, 2003 (Ex. 5), notifying Zydus that the FDA had just issued a Notice of Allowance for the claims that have now been granted as the '524 Patent. Par also advised Zydus that Par believed it was highly likely that the Zydus Tablets, if approved by the FDA, would infringe the allowed claims. *Id.* Par asked Zydus to notify Par if it believed the Zydus Tablets would not infringe Par's patent rights and provide the basis for any such belief. *Id.* Par also specifically called out 35 U.S.C. § 295 and the fact that Zydus would bear the burden of proving that its varenicline API is not made using Par's patented purification methods. *Id.*

On June 12, 2023, the FDA approved Zydus's ANDA, and a week later, outside counsel for Zydus responded to Par's letters, stating only that a substantive response would come "in due course." Ex. 8. In response, Par sent Zydus's counsel a letter that same day reiterating its belief that Zydus's newly-approved tablets would infringe the allowed claims. Ex. 9. That letter detailed the bases for Par's beliefs, and again invited Zydus to identify the basis for any belief that it was not using Par's patented manufacturing methods. *Id.* Par also reiterated the applicability of 35 U.S.C. § 295 and enclosed a draft non-disclosure agreement that would allow Zydus to produce information concerning the manufacturing processes to Par's outside counsel only on a confidential basis in order to allow Par's counsel to evaluate whether Zydus is using the claimed manufacturing methods, as is routinely done in Hatch-Waxman Act cases pursuant

to 21 U.S.C. § 355(c)(3)(D)(i)(III). *Id.* Zydus has not responded to that letter, nor has it provided a substantive response to any of Par’s letters.

Just a few weeks ago, with full knowledge of Par’s issued and expected patent rights, Zydus launched its generic varenicline products and began selling them in the United States. Bradley Declaration, ¶ 17. Zydus has never denied infringing Par’s patents, never provided any basis for believing that it is not using Par’s patented manufacturing methods, and never provided Par with any documentation of the processes that it (and/or any third-party API supplier) are using to make the Zydus Tablets or the varenicline API contained in them.

Information about those processes will have been filed with the FDA by way of the Drug Master File (“DMF”) for the varenicline API and the Chemistry, Manufacturing, and Controls (“CMC”) section of the Zydus ANDA, as well as in manufacturing batch records. Dodds Decl., ¶ 26. But, none of those things are accessible to Par, such that Par has no way to confirm Zydus’s suspected infringement without Zydus’s cooperation, which has not been forthcoming. *Id.*, ¶ 35.

ARGUMENT

I. LEGAL STANDARDS

A party seeking a temporary or preliminary injunctive relief “must establish that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest.” *Ramirez v. Collier*, 142 S.Ct. 1264, 1275 (2022) (quoting *Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008)). In weighing these factors, courts apply a sliding scale whereby they determine whether a party has demonstrated whether it is likely to succeed on the merits and has demonstrated it is more likely than not to suffer irreparable harm, then “determines in its sound discretion if all four factors, taken together, balance in favor of granting

the requested preliminary relief.” *Reilly v. City of Harrisburg*, 858 F.3d 173, 179 (3d Cir. 2017).

These same elements also apply to temporary restraining orders. *QVC, Inc. v. Your Vitamins, Inc.*, 714 F. Supp. 2d 291, 297 (D. Del. 2010) (citing *Nutrasweet Co. v. Vit-Mar Enterprises, Inc.*, 112 F.3d 689, 693 (3d Cir.1997)).

II. THE COURT SHOULD TEMPORARILY HALT FURTHER SALES OF THE ZYDUS TABLETS

Applying these standards in cases involving pharmaceutical drug products, this Court and others have granted preliminary injunctions blocking the sale of pharmaceutical products where, as here, there is a likelihood of success on the merits and irreparable harm will result. *See, e.g., Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1371 (Fed. Cir. 2008); *The Research Found. of State Univ. of N.Y. v. Mylan Pharm. Inc.*, 723 F. Supp. 2d 638, 644 (D. Del. 2010); *Everett Labs, Inc. v. Breckenridge Pharm. Inc.*, 573 F.Supp.2d 855, 871 (D.N.J. 2008); *Novartis Pharm. Corp. v. Accord Healthcare Inc.*, No. 18-cv-1043-LPS, 2019 WL 2588450 (D. Del. June 24, 2019). The Court should do the same here. Each factor weighs strongly in favor of granting a temporary restraining order halting further sales of the Zydus Tablets pending a preliminary injunction hearing or expedited trial on the merits. This relief is needed to prevent the immediate, irreparable, and potentially crippling harm that Zydus’s ongoing sales would inflict on Par before it has a chance to vindicate its patent rights.

A. Par Is Entitled to a Presumption Under 35 U.S.C. § 295 that Zydus Is Infringing the ’524 Patent

To satisfy the likelihood of success factor, Par need only show “a reasonable chance, or probability, of winning” which need not be greater than 50%. *Singer Mgmt. Consultants, Inc. v. Milgram*, 650 F.3d 223, 229 (3d Cir. 2011) (en banc); *see also In re Revel*, 802 F.3d at 570-71 (collecting cases and stating that “strong showing” means “significantly better than negligible but not greater than 50%”); *Reilly*, 858 F.3d at 179 n.3 (“We do not require at the preliminary

stage a more-likely-than-not showing of success on the merits because a likelihood [of success on the merits] does not mean more likely than not” (internal quotations omitted).

Zydus is making the Zydus Tablets in India and importing them into the United States. Accordingly, if Zydus is using Par’s patented methods to make those tablets, then that importation, and Zydus’s subsequent sales of the tablets, constitutes infringement of the ’524 Patent:

Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer...

35 U.S.C. § 271(g).

Moreover, “[w]hile the burden typically rests with the patentee to prove infringement, the law makes exceptions.” *Creative Compounds, LLC v. Starmark Labs.*, 651 F.3d 1303, 1314 (Fed. Cir. 2011). In actions alleging infringement of process claims under § 271(g), a rebuttable presumption of infringement arises if (1) “a substantial likelihood exists that the product was made by the patented process,” and (2) “the plaintiff has made a reasonable effort to determine the process actually used in the production of the product and was unable to so determine.” 35 U.S.C. § 295. “The statute on its face is a burden shifting mechanism...When two conditions are met, the statute shifts that burden and requires the alleged infringer to disprove infringement.” *Nutrinova Nutrition Specialties & Food Ingredients GmbH v. Int’l Trade Comm’n*, 224 F.3d 1356, 1359 (Fed. Cir. 2000).

There are sound policy reasons for this: as the Federal Circuit points out, in such cases “the accused infringer is in a far better position to determine the actual manufacturing process than the patentee,” and therefore “fairness dictates that the accused, likely the only party able to obtain this information, reveal this process or face the presumption of infringement.” *Creative Compounds*, 651 F.3d at 1314-15. That policy applies forcefully to the present circumstances.

Par gave Zydus prompt notice of its patent rights before Zydus launched the Zydus Tablets (indeed, even before Zydus was approved to sell its tablets) and Par has done everything it can to try to ascertain whether Zydus is using its patented manufacturing methods, as Par suspects. Zydus's only response was to state that it would respond "in due course" (Ex. 8), but it never did.

1. There Is a Substantial Likelihood that the Accused Tablets Are Made by the Patented Process

Under § 295, "the burden for establishing a substantial likelihood of infringement has been described as less than ... proving successfully at a trial by a fair preponderance of the evidence that a product in question was in fact made by the patented process but would be more than a slight possibility that the product was so made." *Dasso Int'l, Inc. v. MOSO N. Am., Inc.*, No. 17-cv-1574-RGA, 2021 WL 4427168, at *2 (D. Del. Sept. 27, 2021) (quoting *LG Display Co. v. AU Optronics Corp.*, 709 F. Supp. 2d 311, 335 (D. Del. 2010)). "In other words, the patentee need only present evidence that would support a reasonable conclusion that the imported product was made by the patented process." *Id.* The patent holder "need not show that the patented method is the only commercially practical method of manufacture." *Syngenta Crop Protection, LLC v. Willowood, LLC*, No. 15-cv-274, 2017 WL 1133378 at *8 (M.D.N.C. Mar. 24, 2017) (reversed in part on other grounds, *Syngenta Crop Protection, LLC v. Willowood, LLC*, 944 F.3d 1344 (Fed. Cir. 2019)).

Syngenta is instructive as to the type of evidence that courts accept to establish this conclusion. In *Syngenta*, Syngenta presented evidence that the imported product was manufactured by the patented process that included "internal and external testing by several laboratories" along with expert opinion about the commercial reasonableness of the method. 2017 WL 1133378 at *8. The Court credited both the testing evidence and the expert opinion and found it "adequate to make a persuasive showing of substantial likelihood." *Id.* (internal quotation omitted).

Further, the Court there noted that this evidence was even stronger in “the absence of evidence that anyone actually manufactures [the product] by a method different than that claimed” by the asserted patent. *Id.* at *8; *see also id.* at *9 (“Because Syngenta offers significant persuasive evidence of the presence of [compound], consistent with the use of the patented process, and expert testimony opining that the patented process is used, the Court finds Syngenta has shown a substantial likelihood that [the product] is made with the process claimed by the ‘761 Patent”).

Here, Par presents comparable evidence to support its infringement claims. The claims of the ’524 patent are directed to methods of making either varenicline tartrate tablets (claims 1-11 and 18-25) or varenicline tartrate (claims 12-17 and 26-30). In each instance, the independent claims (claims 1, 12, 18 and 26) include four limitations: (1) varenicline tartrate; (2) less than 50 ppm of nitrosamine impurities; (3) mixing varenicline free base with tartaric acid to form varenicline tartrate; and (4) the use of an acid-base treatment to reduce or remove nitrosamine impurities. As explained in detail in Dr. Dodds’ Declaration:

- Varenicline tartrate: the product labelling provided with the Zydus Tablets confirms that they contain varenicline tartrate as the active ingredient (Dodds Decl., ¶ 32);
- Nitrosamine levels: testing by an independent third-party lab confirmed that, as required by the FDA, the Zydus Tablets contain less than 2 ppm of nitrosamines, well within the claimed ranges (*id.*, ¶ 33, 47);
- Mixing: although it is theoretically possible to form varenicline tartrate in some other manner, mixing the free base form of a drug with an acid is by far the most common, the easiest, and most practical way to make the salt form of a drug substance, such that it is highly

likely that Zydus (or its third-party API supplier if applicable)² is forming the varenicline tartrate contained in the Zydus Tablets in the claimed manner (*id.*, ¶ 38); and

➤ Acid-base treatment: all of the available information about the Zydus Tablets is fully consistent with the use of an acid-base treatment step to remove nitrosamine impurities and as compared to the only other published method for manufacturing low nitrosamine varenicline tartrate, the claimed acid-base treatment method is a far simpler, easier, more practical, and more economical method for doing so (*id.*, ¶¶ 39-44).

Thus, as in *Sygenta*, Par has presented both testing and expert testimony about the commercial practicality and economic reasonableness of Par's claimed methods. That evidence demonstrates that Zydus satisfies two of the four limitations of the independent claims (varenicline tartrate and the claimed nitrosamine levels), that it is exceedingly likely Zydus is using the claimed mixing step, and a significant probability that Zydus is also satisfying the final limitation (i.e., use of the acid-base treatment). In the face of Zydus's intransigence, that is more than enough to "support a reasonable conclusion that the imported product was made by the patented process" and thereby satisfy the first prong of § 295. *Dasso Int'l*, 2021 WL 4427168 at *2; *see also Syngenta*, 2017 WL 1133378 at *8.

2. Par Has Discharged its Duty to Make Reasonable Efforts to Obtain Information Regarding the Zydus Process

With respect to the second prong of § 295, Par has indisputably made "a reasonable effort to determine the process actually used in the production" of the Zydus Tablets, but because of

² It is not evident whether Zydus is making its varenicline API in-house or purchasing it from some third-party API supplier. Either way, if the varenicline API in Zydus's Tablets is made using Par's patented methods, then Zydus's importation and sale of those tablets in the United States constitutes infringement under § 271(g).

Zydus's intransigence, it has been "unable to so determine." 35 U.S.C. § 295. Par has scoured publicly available sources for any available information; it has obtained samples of the Zydus Tablets and had them tested; it has written multiple letters to Zydus asking Zydus to confirm or deny whether it is using Par's patented methods and to provide documentation on an outside counsel's eyes' only basis, a practice that is commonly used in Hatch-Waxman Act cases to allow a patent holder to investigate possible infringement before a generic product comes to market;³ and it has retained an expert to assess the likelihood of Zydus's infringement. There is nothing else Par could have done. Par could easily determine whether Zydus is using its patented methods if it had access to the applicable DMF and the CMC sections of Zydus's ANDA, but Par cannot access those documents on its own, and Zydus has ignored Par's requests for such access, even to Par's outside counsel subject to a stringent non-disclosure agreement.

Considering Zydus's refusal to engage with Par, Par's efforts to determine whether Zydus infringes the '524 patent are more than reasonable. *See, e.g. Dasso Int'l*, 2021 WL 4427168 at *6 (finding efforts reasonable where "Plaintiffs sought documentation of the accused process, which [Defendant] did not provide, and sought to inspect at least one Chinese factory, which was opposed by [Defendant]); *Sygenta*, 2017 WL 1133378 at *9 (finding efforts reasonable where they had been "thwarted by [Defendant's] lack of full cooperation and [an] inability to get information from [a Chinese company]"). "Section 295 requires Plaintiffs to make a reasonable effort to determine the process actually used, not that these efforts be successful." *Dasso Int'l*, 2021 WL 4427168 at *6. Par has used every avenue available to it to obtain this information and has been unsuccessful.

³ Par did not file suit under the Hatch-Waxman Act and 35 U.S.C. § 271(e) because the '524 patent did not issue until after the FDA had approved Zydus's ANDA.

Because Par has shown a substantial likelihood of infringement and made reasonable but unsuccessful discovery efforts to obtain information regarding Zydus's manufacturing process, the Court should shift the burden under 35 U.S.C. § 295 to Zydus to show non-infringement of the '524 Patent. Because Zydus has provided no information to rebut that presumption of infringement, Par is likely to succeed on the merits of its infringement claim.

B. Par Will Suffer Substantial Irreparable Harm If Zydus's Sales Continue

After the FDA forced Pfizer to withdraw CHANTIX® from the market, Par had, for a time, *de facto* market exclusivity with effectively 100% of the varenicline market. Bradley Decl., ¶¶ 9-10. Par was the first, and at that time only, manufacturer who had successfully manufactured varenicline tablets that met the FDA's acceptable daily intake limit for nitrosamine impurities, and Par was able to safely and reliably supply varenicline tablets sufficient to satisfy the market demand from all of its customers for this important drug. *Id.* Varenicline tablets are Par's second largest and second most profitable product, generating nearly [REDACTED] of parent company Endo's company-wide revenue, accounting for roughly [REDACTED] of Endo's company-wide EBITDA ("earnings before interest, taxes, depreciation, and amortization"). *Id.*, ¶ 10. Revenues from the sale of varenicline tablets are critical to Par's and Endo's business, including their ability to invest in research and development for new or reformulated pharmaceutical products, invest in the launch of new products and the growth of existing products, pay employee salaries, and sustain the day-to-day operations of the companies. *Id.* Indeed, now is a particularly tenuous moment in the companies' history, as they are amid voluntary bankruptcy proceedings and hope to emerge from those proceedings by the end of the year. *Id.* ¶ 5. Endo's ability to maintain (and hopefully grow) its revenues and cash flow is an important factor in the success of those plans. *Id.*

Because the Zydus Tablets and Par's tablets are both generic varenicline products approved as therapeutically equivalent to Pfizer's prior CHANTIX® product, the two are entirely substitutable for one another, and any sales of Zydus Tablets necessarily represents lost potential revenue to Par and Endo. *Id.*, ¶ 18. Consequently, if unchecked, Zydus' ongoing sales would inflict wide-ranging, multi-faceted, long-term, corporate-wide harm on Par and Endo. *Id.*, ¶¶ 15-30. Zydus has already been in contact with Par's key customers for varenicline tablets and placed bids at lower prices to gain market share. *Id.*, ¶ 18. Although Zydus has only been on the market for a brief time (just over a month), Par has already begun to feel the effect of its entry and will need to further reduce its pricing in order to maintain any market share if Zydus sales continue. *Id.* Indeed, Par projects that if Zydus is permitted to continue to sell its products unchecked, there will be further additional price erosion, an effect that will only increase with time. *Id.* Such further price erosion may well be unrecoverable. *Id.* at ¶ 19. And that precipitous loss of revenue could have dramatic ripple effects, including impairment of Par's and Endo's investments in R&D, planned sales and marketing efforts for new products, and Par's ability to pay down debt and their cost of capital. *Id.* ¶¶ 24-30. These impacts are inter-related and intertwined, in that negative impacts in any one of these areas will have compounding ripple effects that negatively affect the others and radiate throughout Par, Endo, and Endo's other subsidiaries, such that the full extent of these ripple effects would be both incalculable and irreversible. *Id.* These harms are even starker in light of Endo's ongoing bankruptcy proceedings. *Id.* at ¶ 5.

Courts recognize that pharmaceutical manufacturers suffer these types of harms upon the onset of generic competition and that these harms are irreparable and support entry of preliminary injunctive relief. *See, e.g., Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1361-62,

1371 (Fed. Cir. 2008); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382-84 (Fed. Cir. 2006); *AstraZeneca LP v. Apotex*, 633 F.3d 1042, 1063 (Fed. Cir. 2010). Indeed, when a party sells product to customers who would have otherwise purchased the patentee's product and does so at a discount that creates price erosion, irreparable injury occurs. *Curlin Med. Inc. v. Acta Med., LLC*, 228 F. Supp. 3d 355, 361-62 (D.N.J. 2017) (finding irreparable harm due to price erosion and granting preliminary injunction); *see also Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930 (Fed. Cir. 2012) ("Price erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm"). And courts may consider these harms irreparable even when the defendant's product is already present in the marketplace and price erosion has begun. *See, e.g., Everett Labs.*, 573 F.Supp.2d at 867-69 (finding irreparable harm due to the ongoing price erosion caused by the defendant's product in the market). These harms are particularly acute for Par and Endo, given their fragile financial condition. "There can be no doubt that [this] loss of market share, sales, and business opportunities constitutes irreparable harm." *Edwards Lifesciences AG v. CoreValve, Inc.*, 2014 WL 1493187, at *5 (D. Del. Apr. 15, 2014).

Courts have also found the related, incalculable ripple effects from such losses of revenues to be irreparable harm supporting injunctive relief, including where lost revenues "required [plaintiff] to reduce its research and development activities." *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1566 (Fed. Cir. 1996); *see also Abbott Labs.*, 544 F.3d at 1362 ("loss of [] research and development support constitute[s] irreparable harm"); *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 609 F. Supp. 2d 786, 812 (S.D. Ind. 2009) (irreparable harm from "a scaling back of investment in research and development which otherwise would not have occurred").

An order temporarily halting further Zydus sales is necessary to avoid these harms and give Par a fair opportunity to pursue its infringement claims. If Zydus produces the manufacturing information that is undoubtedly readily available to it, and that documentation shows that it is not using Par's patented methods, the temporary restraining order can be lifted and Zydus can resume sales. Zydus should not be permitted to inflict massive harm on Par while it stonewalls Par's efforts to confirm Zydus's suspected infringement. Given Endo's precarious financial condition, delayed justice will be no justice at all.

C. The Balance of the Hardships Favors Granting the Requested Injunction

Because “[Par] will suffer irreparable harm absent an injunction, the balance of equities weighs strongly in [Par's] favor.” *See Nevro v. Stimware Techs., Inc.*, No. 19-325, 2019 WL 3322368, at *16 (D. Del. July 24, 2019). Moreover, the hardship Par would suffer far exceeds the consequences to Zydus of returning to the status quo prior to Zydus's launch.

First, the harms inflicted on Par—e.g., price erosion, lost R&D opportunities, impaired promotion of new and early-stage products, etc.—will be severe and irreversible. Bradley Decl. at ¶¶ 18-30. By contrast, Zydus knows whether it is using Par's patented manufacturing methods, and if it is not, Zydus could end this matter immediately—and could have ended it a month ago—by producing the relevant portions of the DMF and its ANDA demonstrating that that is so. However, Zydus chose a different path and has refused to engage with Par. Zydus's decision to launch with knowledge of Par's patent rights and blithe disregard for Par's reasonable inquiries is on Zydus, not Par, and “any harms that [Zydus] may face...are attributable to its own at-risk conduct.” *Everett Labs.*, 573 F. Supp. 2d at 870 (citing *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006)).

Second, Par's hardships will be incalculable. Ongoing Zydus sales would cause multifaceted, long-term harms to Par's varenicline franchise, including price erosion and lost market share, and potentially to the company as a whole, including Par's and Endo's other operating subsidiaries. Bradley Decl. at ¶ 28-32. In contrast, any potential loss of profits Zydus would experience due to an injunction "are quantifiable, more so and more easily than the harms [Par] will suffer." *Research Found. of the State Univ. of N.Y. v. Mylan Pharm. Inc.*, 723 F. Supp. 2d 638, 660-62 (D. Del. 2010). And the potential harm to Zydus is in the form of delayed profits, not profits that are forever lost and risks to the company as a whole.

Third, Par's hardships, though unquantifiable, will be substantial. In 2022, varenicline tablets generated revenues of [REDACTED] million, and those revenues accounted for [REDACTED] of Endo's company-wide EBITDA. Bradley Decl. at ¶ 10. Consequently, varenicline revenues are important to Par's and Endo's ability to fund and support their planned business operations. The harm resulting from such a large, precipitous drop in revenues would be particularly acute considering Endo's ongoing bankruptcy proceedings and efforts to reorganize. *Id.* at ¶ 5. In short, Zydus would not face the same kind of structural harm if the requested temporary relief is granted that Par would suffer if it is not. *See, e.g., Par Pharm., Inc. v. TWI Pharm., Inc.*, No. 11-cv-2466, 2014 WL 3956024, at *5 (D. Md. Aug. 12, 2014).

Finally, the requested injunction, if granted, will be "only if the movant gives security in an amount that the court considers proper to pay the costs and damages sustained by any party found to have been wrongfully enjoined or restrained." Fed. R. Civ. P. 65(c). The security provided should be set for an amount sufficient to cover the lost profits Zydus may suffer pending a judgment on the merits. *See, e.g., Research Found.*, 723 F.Supp.2d at 662 ("In this

way, the bond mitigates the harms that Mylan will suffer”). Zydus will be compensated should it be determined that the temporary restraints were improvidently entered.

D. An Injunction Is in the Public Interest

The public interest favors an injunction. There is a “significant public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid pharmaceutical patents.” *Abbott Labs.*, 544 F.3d at 1362-63 (internal quotation marks omitted). Any public benefit Zydus attributes to selling its infringing product is outweighed by “the public interest in recognizing [Par’s] patent rights, and more generally promoting continued, large-scale investment in research and development of new pharmaceuticals.” *Research Found.*, 723 F. Supp. 2d at 663. Indeed, public policy does not support “eliminating the exclusionary rights conveyed by pharmaceutical patents” or “excuse infringement of valid pharmaceutical patents.” *Everett Labs.*, 573 F. Supp. 2d at 870-71. Thus, the public interest in allowing Par’s case to be heard outweighs the temporary delay in availability of potentially cheaper drugs.⁴

III. THE COURT SHOULD GRANT EXPEDITED DISCOVERY IN ADVANCE OF A PRELIMINARY INJUNCTION OR EXPEDITED TRIAL ON THE MERITS

As Par’s argument above makes clear, the key question on the merits of Par’s infringement claim is exactly what method Zydus is using to make the Accused Tablets. Par has taken advantage of all reasonable methods available to it to determine what that method is, but in light of Zydus’ intransigence, it has been unable to do so. Accordingly, Par seeks expedited discovery, in advance of the proposed preliminary injunction hearing, limited to one simple question: how does Zydus make its tablets and the varenicline API included in them.

⁴ There is currently one other varenicline product on the market, an Apotex generic. Accordingly, generic competition will still exist following an injunction against Zydus.

“[C]ourts have regularly noted that expedited discovery is more likely to be an efficient use of the parties’ resources when it relates to a pending preliminary injunction hearing, where it can help to ensure a clear and focused factual record.” *Kone Corp. v. ThyssenKrupp USA, Inc.*, No. 11-cv-465-LPS-CJB, 2011 WL 4478477, at *7 (D. Del. Sept. 26, 2011). For this reason, courts have found that the circumstances of a case weigh in favor of granting expedited discovery “particularly insofar as that discovery directly relates to disputed facts at issue regarding [a preliminary injunction] motion.” *Id.* at *6 (finding good cause existed to grant limited expedited discovery in advance of a possible preliminary injunction); *see also Croft v. Donegal Township*, No. 20-cv-01430, 2020 WL 6803051, at *3 (W.D. Pa. Nov. 19, 2020) (ordering that “[t]he parties may engage in limited discovery to prepare for the preliminary injunction hearing”).

Par seeks a limited set of documents and 30(b)(s) deposition. *See* Ex. 11 and proposed order submitted herewith. These requests are narrowly tailored to a singular goal: obtaining discovery on the methods that Zydus (and/or any third-party API manufacturer) are using to make the Zydus Tablets and API contained in them. This discovery will aid the parties and the Court in preparing for a preliminary injunction hearing or expedited trial on the merits so that the Court may determine the proper scope of such an injunction.

IV. CONCLUSION

The Court should temporarily halt Zydus’s ongoing sales of the Zydus Tablets, order Zydus to produce expedited discovery concerning its manufacturing processes, and schedule a preliminary injunction hearing or expedited trial on the merits to assess whether Par is entitled to further preliminary or permanent injunctive relief.

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